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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
LI, QIAN JANICE

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,835	CHANCELLOR ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) *1-20 and 23-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,22 and 38-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5/02 10/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II (claims 21, 22, 38-63), and species election drawn to a combination of muscle stem cells (MDS) and small intestine submucosa (SIS), is acknowledged. The traversal is on the ground(s) that the claims are related as being a composition and a process of making, and that a search of these claims can be made without serious burden. This is not found persuasive because it is maintained that each of the Inventions requires a separate search status and consideration. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the composition of group II could be made by another and materially different process such as the method of group III of instant application, or the method taught in US patent 6,022,743. Further, the patentability of a product claim is determined by the novelty and nonobviousness of the claimed product itself without consideration of the process for making it. *In re Thorpe*, 227 USPQ 964 (Fed. Cir. 1985). The searches for groups II and I would have certain overlap, but they are not co-extensive. M.P.E.P. states, "FOR PURPOSES OF THE INITIAL REQUIREMENT, A SERIOUS BURDEN ON THE EXAMINER MAY BE PRIMA FACIE SHOWN IF THE EXAMINER SHOWS BY APPROPRIATE EXPLANATION OF SEPARATE CLASSIFICATION, OR SEPARATE STATUS IN THE ART, OR A DIFFERENT FIELD OF SEARCH AS DEFINED IN MPEP § 808.02". Moreover, in the

previous Office action for restriction, the Office has clearly indicated where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product clam will be rejoined in accordance with the provisions of MPEP § 821.04. Therefore, it is maintained that these inventions are distinct due to their divergent subject matter. Further search of these inventions is not co-extensive, as indicated by the separate classifications. The requirement is still deemed proper and is therefore made **FINAL**.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Claims 1-63 are pending, however, claims 1-20, and 23-37 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 21, 22, 38-63 are under current examination. Applicant is reminded that where generic claims encompass more than one species as defined in the previous Office action, upon election of a species for examination, said claim will only be examined to the extent that it reads upon the elected species, i.e. a composition or preparation comprising MDS and SIS, there being no allowable generic or linking claim.

Claim Objection

Claim 45 is objected to because claim recitation "further" should be deleted.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The language should be clear and concise and should not repeat information given in the title. It should *avoid* using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure *describes*," etc.

The abstract of the disclosure is objected to because it uses the phrase "describes" or "described". Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 22, 38-63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using a graft composition comprising autologous muscle stem cells and a matrix material for tissue repair, wherein the tissue to be repaired is selected from the group consisting of smooth muscle, skeletal muscle, skin and connective tissue, bladder, and blood vessels, does not reasonably provide enablement for using allogenic and xenogenic muscle stem cells

for repairing any tissue or organ. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention are summarized in *In re Wands*, (858 F2d 731, 737, 8 USPQ 2d 1400, 1404, (Fed Cir.1988)). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided. The factors most relevant to this rejection are the scope of the claims relative to the state of the art and the levels of the skilled in the art, and whether sufficient amount of direction or guidance are provided in the specification to enable one of skill in the art to practice the claimed invention.

Given the broadest reasonable interpretation, the claims encompass using MDS for repairing any tissue and organ as recited in claim 61. These claims clearly or implicitly state the intended use of the composition. With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. "WHEN A COMPOUND OR COMPOSITION CLAIM IS LIMITED BY A PARTICULAR USE, ENABLEMENT OF THAT CLAIM SHOULD BE EVALUATED BASED ON THAT USE". (MPEP 2164.01c) When analyzing the enabled scope of the claims, the intended use is to be taken into account because the claims are to be given their

broadest reasonable interpretation that is consistent with the specification. Therefore, the claims will be evaluated by that standard.

In view of the guidance provided, the specification illustrated obtaining the MDS cells from rat, and using the MDS-SIS preparation for skin wound, and suburethral sling. The art of record such as *Vandenburgh et al* (US 6,503,504) teach obtaining MDS from mice for tissue repair, and the SIS has been shown for augmentation of bladder or vessel graft (*Knopp et al*, J Urology 1996;155:2098-2104; and *Baltoyannis et al*, Intl Angiol 2000;280-4). However, neither the art of record nor the specification discloses that MDS could differentiate to other cell types other than muscle and connective tissue, such as liver, lung, and blood cells. Assuming the MDS does have the potential to differentiate to all types of body cells, the specification fails to teach how to induce the MDS differentiate to only the cell type of interest. Thus, the specification fails to provide an enabling disclosure to support the full scope of the claims.

In view of the state of the art of stem cell technology, it is not well developed and highly unpredictable. *Watt et al* (Science 2000 Feb;287:1427-30) review the infant stage of the stem cell biology, "THE SPOTLIGHT ON STEM CELLS HAS REVEALED GAPS IN OUR KNOWLEDGE THAT MUST BE FILLED IF WE ARE TO TAKE ADVANTAGE OF THEIR FULL POTENTIAL..., WE NEED TO KNOW MORE ABOUT THE INTRINSIC CONTROLS THAT KEEP STEM CELLS AS STEM CELLS OR *DIRECT THEM ALONG PARTICULAR DIFFERENTIATION PATHWAYS.*" *Donovan and Gearhart* (Nat 2001 Nov;414:92-97) teach "IF STEM CELLS ARE TO BE USED TO TREAT A WIDE VARIETY OF HUMAN DISEASES, THEN WE WILL NEED TO OVERCOME SEVERAL FORMIDABLE CHALLENGES. STEM CELLS WILL BE NEEDED IN LARGE QUANTITIES AND BE ABLE TO DIFFERENTIATED IN A CONTROLLED MANNER TO FORM HOMOGENEOUS POPULATIONS OF CELLS THAT ARE HISTOCOMPATIBLE WITH AN

INDIVIDUAL" (left column on page 95). The specification fails to teach how to overcome the aforementioned difficulties in the art. It would have required undue experimentation for the skilled artisan intending to practice the instant invention.

Claims further encompass using the composition as allograft and xenograft. With this aspect, there are still major barriers for successful transplantation as of the instant filing date. *Game et al* (Wien Klin Wochenschr 2001;113:823-38) detailed different types of allogenic and xenogenic rejection (hyperacute, acute, chronic) and underlying mechanisms involving multiple pathways that lead to the failure of allogenic and xenogenic transplantation, and states, "WHILE MAJOR IMPROVEMENTS HAVE BEEN MADE IN THE PREVENTION AND TREATMENT OF HYPERACUTE AND ACUTE TRANSPLANT REJECTION, MOST GRAFTS WILL SUCCUMB TO CHRONIC REJECTION: THIS REFLECTS THE EXTENT OF OUR KNOWLEDGE OF THE MECHANISMS THAT DRIVE THESE PROCESSES", as for xenotransplantation, "NOVEL APPROACHES HAVE OVERCOME SOME EARLY ANTIBODY MEDIATED REJECTION EVENTS BUT THEN REVEAL A HUGE, INTENSE, ADAPTIVE CELLULAR RESPONSE". *Platt et al* (Nat Biotech 2002 Mar;20(3)231-2) clearly teach, "UNFORTUNATELY, SOLVING THE PROBLEM OF HYPERACUTE REJECTION DOES NOT MAKE XENOTRANSPLANTATION FEASIBLE, BUT RATHER REVEALS A MORE VEXING PROBLEM CALLED ACUTE VASCULAR REJECTION. ACUTE VASCULAR REJECTION, LIKE HYPERACUTE REJECTION, IS TRIGGERED BY ANTI-DONOR ANTIBODIES; HOWEVER, IN CONTRAST TO HYPERACUTE REJECTION, THESE ANTIBODIES ARE NOT DIRECTED EXCLUSIVELY AGAINST α1,3GAL, AND THE INVOLVEMENT OF THE COMPLEMENT SYSTEM IS FAR MORE SUBTLE". With respect to muscle stem cells, *Qu et al* (J Cell Biol 1998;142:1257-67) teach that myoblast (MDS) transplantation has been extensively studied as a treatment approach for muscular disease, however, it has been hindered by numerous limitations including immunoloical problems, low spread and

poor survival of injected myoblasts (e.g. abstract). Thus, it is evident that at the time of the invention, the skilled artisan in the relevant art, while acknowledging the significant potential of stem cell therapy, still recognized that such therapy was neither routine nor accepted, and awaited significant development and guidance for its practice. Therefore, it is incumbent upon applicants to provide sufficient and enabling teachings within the specification for such therapeutic regimen. Although the instant specification provides a brief note of a potential therapeutic use of the claimed cells, it is not enabled for its full scope because the specification fails to provide support for the full scope of the claims.

The claims further encompass obtaining muscle stem cells from embryo. However, the specification fails to teach how to obtain them from an embryo where the muscle has yet to develop. With respect to use of embryonic stem cells, *Odorico et al* (Stem Cells 2001;19:193-204) detailed the major barriers for using EM stem cell lines for routine therapeutic purpose in addition to the danger of immune rejection. They teach that the efforts have been hampered a). by the inability to selectively differentiating human ES cells to a particular cell type of interest and to purify this lineage from the mixed population; b). by the inability to demonstrate that the differentiated cells and cellular derivatives function in a normal physiologic way, because differentiated ES cell cultures can contain multipotent progenitors as well as terminally differentiated cells. Many fetal or embryonic tissues and multipotent cells are functionally immature, one cannot assume that all ES cell progeny will subserve normal cellular physiologic functions; c). by the requirement of integration of the transplanted cells into the existing host tissue in a functionally useful form; d). by the possibility that

human ES cell derivatives may form tumors in human recipients (see particularly, pages 198-200). The specification fails to teach how to overcome the aforementioned difficulties in the art. It would have required undue experimentation for the skilled artisan intending to practice the instant invention.

Accordingly, based upon the limited disclosure, the unpredictability of the art, the level of the skill, and the breadth of the claims, one skill in the art would have been required to perform undue experimentation to practice the invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims are vague and indefinite because of claim recitation, "innervatable". The specification does not define the term, and the term can not be found in a standard English dictionary. It is unclear the meaning of the term, thus, the metes and bounds of the claims are uncertain.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(f) he did not himself invent the subject matter sought to be patented.

Claims 21, 22, 38, 40-44, 46-56, 61 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 09/549,937 which has a common assignee and inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if published under 35 U.S.C. 122(b) or patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future publication or patenting of the copending application.

Claim 115 of the cited application is drawn to a physiological acceptable composition comprising muscle derived stem cells and a carrier, wherein the cells are autologous or allogenic, in the amount of 1X106, for example (page 22, line 8), and the specification teaches that the carrier could be a collagen sponge matrix material (page 18, line 24), which is a physiologically acceptable matrix material or implantable substrate material in a three-dimensional scaffolding. Accordingly, the cited patent application anticipates instant claims.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131. This

rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

Claims 21, 22, 38, 40-44, 46-56, 61 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The cited patent application 09/549,937 and the instant claims are drawn to the same subject matter, but the cited application has a different inventive entity. It is unclear as to who is the real inventor.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21, 22, 38-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Ye et al* (Eur J Cardio-Thorac Surg 2000 April;17:449-54), or *Ataka* (US 6,482,645) or *Vandenburgh* (US 6,503,504), in view of *McDowell et al* (US 6,171,340), and *WO*

99/56785, and as evidenced by *Capelli et al* (US 5,045,601) and *Humes et al* (US 2002/0090389).

Ye et al teach a composition comprising autologous human muscle stem cells (myofibroblasts) obtained from ascending aorta cultivated on aortic tissue sheet (matrix material), forming a three-dimensional implantable scaffold for pericardium implantation. *Ye et al* also teach other art known matrix material that could be used for cell growth support (paragraph bridging pages 449-50), but do not mention SIS.

Ataka teaches a composition (artificial fascial slings) comprising biocompatible substrates (column 4, § I) and muscle stem cells (column 5, § II, line 41-42), and using such for treating urinary incontinence, wherein the cells are preferably autologous (column 5, line 20). *Ataka* does not teach that the substrate is SIS or the amount of muscle cells.

Vandenburgh teaches a composition comprising muscle stem cells (e.g. fig. 2) in an extracellular matrix suspension (e.g. abstract), and a vessel having a three dimensional geometry (fig. 1), wherein the muscle stem cells cultured in the vessel, and an implantable three-dimensional scaffolding would form simulating the *in vivo* tissue morphology (e.g. abstract) and having muscle contractility and could be used for tissue repair (e.g. fig 8), wherein the MDS were seeded 1-4x10^6 cells per vessel (column 10, line 52), and wherein the MDS are isolated from skeletal muscle (e.g. column 22, § G). *Vandenburgh* does not teach using SIS as the matrix in the preparation.

McDowell et al teach a composition for repairing damaged joint comprising stem cells (column 6, line 22) and a substrate that may enhance tissue growth (column 6,

lines 45-62), wherein the substrate could be SIS (a polymer derived from small intestineal submucosa), wherein the cells for transplant may be attached to shield or spacer before transplantation, wherein the shield and spacer serve as an anchor or scaffold to which the cells attach (column 6, lines 24-26), or the cells for transplant may be inserted into the substrate material (column 6, lines 61-62). Although *McDowell et al* do not specify how the cells are attached to the scaffold, using adhesive for medical product is well known in the art as evidenced by *Capelli et al* who teach a dermatologically acceptable adhesive that could be used in medical products, and *Humes et al* who use fibrin glue for delivering stem cells (hydrogel-cell suspension, paragraph 0135). Although *McDowell et al* do not teach specifically the muscle stem cells, such has been taught by *Ye et al*, *Ataka, Vandenburgh, and WO 99/56785.*

WO 99/56785 teach muscle derived stem cells for tissue repair (e.g. abstract), wherein the stem cells are preferably autologous (page 14, line 13), wherein the cells are obtained from skeletal muscle (page 23, line 26), wherein the stem cells were injected into urethral wall as treatment for urinary stress incontinence (example 2), and the detrusor contractility (the major contractile muscle of the bladder) was improved (example 3).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Ye et al*, *Ataka* or *Vandenburgh*, *WO 99/56785,* and *McDowell et al* by simply using muscle stem cells as the type of stem cells, and SIS as the type of substrate to make a tissue repair composition with a reasonable expectation of success. Given the types of stem cells

known in the art, and the type of biocompatible matrix materials known in the art, it is within the knowledge of the reasonably skilled in the art to select the stem cell of interest combined with the matrix material available for tissue repair.

It would also have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Ataka* or *Vandenburgh* and *McDowell et al* by anchoring the muscle stem cells either on a shield carrier or a SIS carrier with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because depending on the type of tissue to be repaired, a shield or a SIS may be more suitable for implantation.

Although none of the cited references specify the amount of stem cells seeded on the matrix as recited in claim 56, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the amount of cells should be used for seeding. Given the state of the art in tissue culture technology, this limitation would fall within the bounds of optimization.

Although *MacDowell et al* do not specify the timing of stem cell attachment to the anchoring material, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine an appropriate time for attachment before transplantation. Given the levels of the skilled in the art of transplantation, these limitations (claims 57-59) would fall within the bounds of optimization.

Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 21, 22, 46-56, 59-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over *WO 99/56785,* in view of *Kropp et al* (J Urol 1996;155:2098-2104), *Vandenburgh* (US 6,503,504), and *McDowell et al* (US 6,171,340).

WO 99/56785 teach muscle derived stem cells for tissue repair (e.g. abstract), preferably urinary system injury (example 2), wherein the stem cells are preferably autologous (page 14, line 13), wherein the cells are obtained from skeletal muscle (page 23, line 26), wherein the stem cells were injected into urethral wall as treatment for urinary stress incontinence (example 2), and the detrusor contractility (the major contractile muscle of the bladder) was improved (example 3). *WO 99/56785* do not teach combining the stem cell transplant with a SIS matrix, and admix them right before implantation.

However, before the instant effective filing date, *Kropp et al* use SIS as a scaffold for regenerative surgery of urinary bladder, and concluded that it is an option for bladder reconstruction.

As discussed above in detail, *Vandenburgh* and *McDowell et al* teach that in tissue repair, there are multiple approaches for transplanting the stem cells and substrate material depending on the need of the tissue to be repaired, they could be co-cultured or attached together, and transplanted alone or in combination.

Evidently, it is well known in the art that either the muscle stem cells or the SIS could be used effectively for tissue repair, *alone or in combination*, such as in bladder reconstruction. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the two means to form a new

composition for tissue repair with a reasonable expectation of success, wherein the two components could be attached together or just apply at the same time. The ordinary skilled artisan would have been motivated to modify the claimed invention because two means would enhance tissue regeneration since they address different aspects of restoration, i.e. the SIS as a scaffold and MDS as a cell-renewing source. Thus, the claimed invention as a whole was clearly *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21, 22, 38, 40-44, 46-56, 61 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 115 of U.S. Patent No. 09549,937. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the present and cited applications are each drawn to a physiological acceptable composition comprising

muscle derived stem cells and a carrier, wherein the cells are autologous or allogenic, in the amount of $1X10^6$, for example (page 22, line 8), and the specification teaches that the carrier could be a collagen sponge matrix (page 18, line 24), which is a physiologically acceptable matrix material or implantable substrate material in a three-dimensional scaffolding for tissue repair. Accordingly, the claims of the present and cited patent applications are obvious variants and co-extensive.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist **Rena Jones** whose telephone number is **571-272-0571**.

Q. Janice Li
Patent Examiner
Art Unit 1632

QL
April 1, 2004

JANICE LI
PATENT EXAMINER